--35. The compound according to claim 34, wherein the compound is N,N-diethyl-2-cyano-3-(3,4-dihydroxy-5-nitrophenyl)acrylamide.

--36. The compound according to claim 34, wherein the compound is selected from the group consisting of 2-cyano-3-(3,4-dihydroxy-5-nitrophenyl)acrylamide, N,N-dimethyl-2-cyano-3-(3,4-dihydroxy-5-nitrophenyl)-acrylamide and N-isopropyl-2-cyano-3-(3,4-dihydroxy-5-nitrophenyl)-acrylamide.--

REMARKS

Entry of the foregoing and reconsideration of the subject application in light of the following comments are respectfully requested.

At the outset, Applicants wish to indicate that a new Abstract is attached hereto which more particularly relates to the claimed invention.

The specification has also been amended to recite a "Brief Description of the Drawings" on page 2 of the specification.

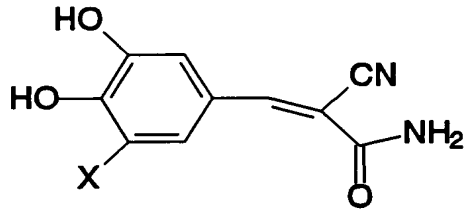
In a telephone conversation with one of Applicants' representatives on November 16, 1993, a provisional election of the species recited as the second species of claim 32 was elected with traverse. Applicants wish to maintain at the outset that in view of the discussion set forth below, all of the species in amended claim 29 should be considered in the subject application. Applicants understand that all species in claim 29 have been searched and, as such, Applicants maintain that amended claim 29 as well as claims 30-32 and new claims 33-36 are now in condition for allowance.

Applicants note with appreciation that claims 31 and 32 are objected to as depending on a rejected base claim. Claims 31 and 32 have now been amended to place them in independent form and they are now in condition for allowance.

There is only one rejection of record. Claims 29 and 30 have been rejected under 35 U.S.C. §103 as allegedly being unpatentable over Lauerer et al, U.S. Patent No. 3,278,448. This rejection is respectfully traversed.

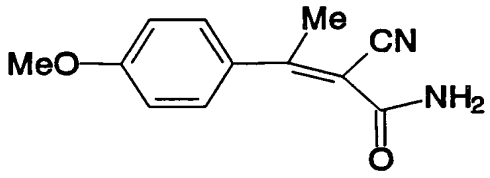
At the outset, Applicants wish to emphasize that independent claim 29 has now been amended such that the position of the electronegative Group X is fixed at the 5-position of the aromatic ring. As noted in Table 1 on pages 15 to 18 of the specification, the compounds wherein X is in the 5-position are clearly better than the compounds wherein X is in the 6-position. In this regard, Applicants would like to specifically direct the Examiner's attention to the IC_{50} values of the compounds of Examples 24 and 41. The IC_{50} for each of those examples are set forth on page 17 of the specification. In particular, the IC_{50} value for the compound of Example 24 is 90 while the IC_{50} value for the compound of Example 41 is 380. The IC_{50} is the concentration of drug which inhibits 50% of the catechol-O-methyltransferase activity. The compounds of the present invention are especially advantageous since they effectively inhibit the enzyme at low concentrations. Thus, the compounds wherein X is in the 5-position is clearly better than the compounds wherein X is in the 6-position.

The present invention is directed to disubstituted catechols of formula I which include 3,4-dihydroxy-5-halogeno-α-cyano-cinnamic acid amide derivatives of the following formula:



The above-mentioned compound may fall, in a general way, within the scope of the type of compounds disclosed in Lauerer et al. However, Lauerer et al fails to appreciate or even to suggest that the number of hydroxy groups have to be exactly two and that the hydroxy groups must be in the meta and para positions of the side chain containing the amide group of the benzene ring. Further, Lauerer et al fails to state that the presence of the halogeno group next to the 4-hydroxy group is essential. Lauerer et al simply states that the presence of the halogeno group is optional and no information is offered or suggested concerning its position on the aromatic ring.

Applicants believe that the closest compound of Lauerer et al is



This compound is the only compound among the specific compounds listed in Lauerer et al which contains an amide group in the side chain. The Lauerer et al compound does not have very much in common with the compounds of the presently claimed invention. In particular, the Lauerer et al compound does not contain any hydroxy groups, thus, the compound is not a catechol derivative. In addition, the electronegative group is not

present. Further, there is a methyl group in the side chain which the compounds of the present invention do not possess.

Thus, Applicants maintain that the compounds of newly amended claim 29 are not anticipated by nor made obvious over the disclosure of Lauerer et al. Applicants' compounds possess an unexpectedly superior advantage with respect to the inhibition of catechol-O-methyltransferase. Accordingly, the rejection of claims 29 and 30 under 35 U.S.C. §103 as being unpatentable over Lauerer et al should be withdrawn.

Applicants also wish to point out that they have introduced new composition of matter claims 33-36 in the subject application. Lauerer et al fails to disclose any pharmaceutical activity whatsoever as to any of their disclosed compounds. Lauerer et al directed their attention to ultraviolet light filters. Such compounds absorb ultraviolet rays and no pharmaceutical utility is disclosed.

In view of the foregoing, a Notice of Allowance is respectfully requested.

Should the Examiner have any questions concerning the subject application a telephone call to the undersigned would be appreciated.

Respectfully submitted,

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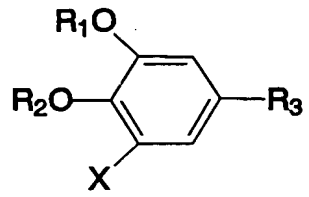
08/121617

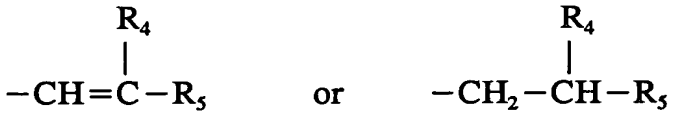
ABSTRACT OF THE DISCLOSURE

A compound according to formula 1



I

wherein R_1 and R_2 independently represent hydrogen, carbamoyl which is substituted by an alkyl of 1 to 4 carbon atoms, alkylcarbonyl of 2 to 5 carbon atoms or phenyl carbonyl, X represents halogen nitro or cyano and R_3 represents



or

wherein R_4 represents cyano or alkylcarbonyl of 2 to 5 carbon atoms and R_5 represents carbamoyl which is unsubstituted or substituted with alkyl of 1 to 8 carbon atoms or which is substituted with hydroxyalkyl of 1 to 8 carbon atoms or pharmaceutically acceptable esters and salts thereof, and a pharmaceutically acceptable carrier therefor, as well as pharmaceutical compositions containing said compounds as COMT inhibitors.